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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,511	10/31/2003	George Nelson Bennett	61683-00002USPT	3571

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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/699,511	**Applicant(s)** BENNETT ET AL.	
	Examiner Heather G. Calamita, Ph.D.	**Art Unit** 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 September 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *26 September 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-7*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s) _____
13. ☐ Other: _____.

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Art Unit 1637

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue none of the cited art shows "simultaneously removing and circularizing" assembled PCR fragments from a solid support with a recombinase. This argument is not persuasive because there is strong suggestion in the prior art that the combination of these technologies, specifically assembly of DNA fragments on a solid support and simultaneous removal recombination and circularization of the DNA would be successful. Additionally, the federal circuit held in Pharmastem Therapeutics, Inc. v. Viacell, Inc., __ F.3d __ (Fed. Cir. 2007) a treatment method to be obvious citing the following:

1) KSR followed - Confirmation of Stem Cell Properties Obvious: The invention was novel in the sense that it was not confirmed in the prior art that umbilical cord blood is capable of hematopoietic reconstitution. Relying upon KSR, the court majority stated that "[w]hile the inventors may have proved conclusively what was strongly suspected before - that umbilical cord blood is capable of hematopoietic reconstitution - and while their work may have significantly advanced the state of the science of hematopoietic transplantations by eliminating any doubt as to the presence of stem cells in cord blood, the mouse experiments and the conclusions drawn from them were not inventive in nature. Instead, the inventors merely used routine research methods to prove what was already believed to be the case. Scientific confirmation of what was already believed to be true may be a valuable contribution, but it does not give rise to a patentable invention."Applicant argues the previously submitted declaration provides evidence as to unexpected results. This declaration was not persuasive because the declaration failed to provide persuasive evidence as to unexpected results. It is well established in the art that Cre/Lox recombinase will simultaneously recombine and circularize plasmid DNA. It is therefore not unreasonable to expect success when using Cre/lox to simultaneously recombine and circularize DNA which is attached to a substrate. Applicants argue the topology of DNA is affected by binding to a solid support which affects recombinase activity and that topology is known to be critical to recombinase function. Applicant submitts several papers in support of this assertion. None of these papers support the assertion that by binding DNA to a solid substrate the structure is changed so markedly that recombinase would not function.

Applicant argues a recombinase is not a ligase and the assembly of DNA on a solid support using a ligase is not analoguous and cannot be used to extrapolate success for the applicaton of recombinase. This argument is not persuasive because the issue is reasonable expectation of success. There is a reasonable expectation of success because the prior art directly points to the assembly of PCR products (taught by Watson), that assembly can occur on a solid support (taught by Stahl) and that Cre recombinase provides simultaneous recombination and circularization of plasmid DNA in vitro (taught by Elledge). Applicant asserts that one of skill in the art would have thought Cre/lox recombination was inhibited or impossible on a solid support. Applicant fails to provide evidence to this effect. The prior art of record does not indicate this was thought to be the case as Cre/lox is a well known well used system for in vitro recombination. Additionally with regard to Applicant's request for an affidavit, Examiner notes that there is no basis in MPEP § 2144 which requires the Office to supply an affidavit when the motivation is provided directly in the prior art document(s). None of the facts relied upon in the 103 rejection are the personal knowledge of the examiner. Instead, as noted in the 103 rejection recited above, the motivation is expressly stated within the reference(s). The Examiner at no point in the rejection indicated the use of personal knowledge in finding a motivation to combine between the references. This line of argument is inappropriate. Applicant argues the Examiner must consider the declaratory evidence. This argument is not persuasive as the declaration was considered in the Office Action mailed July 26, 2007. It was noted in the Action that Applicant's declaration failed to provide evidence of unexpected results. Applicants merely assert in the declaration that the function of recombinase is unexpected and fail to provide any data or evidence to support the assertion.